Results: 18 patients with HLA-Ab against UCB unit 1 (9), UCB unit 2 (2) or both UCB units (7) were identified. No differences in cell doses, viability or baseline characteristics were noted between patients with/without HLA-Ab. The presence of HLA-Ab was associated with an increased risk of graft failure (HLA-Ab against either UCB unit: OR 8.67, 95%CI 1.89–39.68, p = 0.0055; HLA-Ab against both UCB units: OR 16.27, 2.82–93.87, p = 0.0034). Neutrophil engraftment was delayed in the presence of HLA-Ab (median 21 vs. 29 days, p = 0.04) and fewer patients engrafted platelets in the presence of HLA-Ab (76.4% vs. 50%, p = 0.03). HLA-Ab against UCB unit 1 was associated with UCB unit 2 dominance (OR 9.43, 95%CI 1.16–76.47, p = 0.015), while HLA-Ab against UCB unit 2 was associated with a non-significant trend toward UCB unit 1 dominance (OR 2.70, 95%CI 0.63–12.5, p = 0.28). Overall survival was inferior in the presence of HLA-Ab against UCB unit 2 (p = 0.044) or both UCB units (p = 0.027), but not with HLA-Ab against UCB unit 1 only.

Conclusions: In DUBCT, the presence of HLA-Ab increases the risk of graft rejection, prolongs time to engraftment, predicts UCB dominance and is associated with inferior outcome. HLA-Ab screening should be incorporated into UCB unit selection strategies in DUCBT.

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EX VIVO TREATMENT OF HEMATOPOIETIC STEM CELLS WITH 16,16-DIMETHYL PROSTAGLANDIN E2 (FT1050) IMPROVES ENGRAFTMENT AND HEMATOPOIETIC RECONSTITUTION

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Through an in vivo zebrafish screen for modulators of hematopoietic stem cell (HSC) development, a small molecule, 16,16-dimethyl prostaglandin E2 (FT1050) was identified (North, 2007). FT1050 was shown to enhance the engraftment potential of HSCs from murine bone marrow (mBM) or human umbilical cord blood (hCB) in murine engraftment models through an increase in proliferation, survival, migration and homing after a brief (1 to 2 hr) ex vivo treatment (North, 2007; North, 2009; Hoggatt, 2009; North, Goessling, Zon, unpublished data). We further optimized the ex vivo hCB incubation protocol using whole genome expression arrays and determined that HSC-containing cell products should be incubated with 10μM FT1050 for 2 hrs at 37°C to obtain the optimal response. In addition, we observed that FT1050 induces similar gene expression changes in hBM- and mobilized peripheral blood-derived CD34+ cells. Subsequent functional studies demonstrated that in keeping with increases of up to 18-fold in CXCR4 gene expression, cell surface CXCR4 protein expression was also significantly increased. One hour after treatment with10μM FT1050 for 2 hrs at 37°C, 48±1.9% of CB CD34+ cells expressed CXCR4 compared to 3.5±0.01% in DMSO control ($p < 0.05$). In vivo CFU-S12 analysis showed that treatment of mBM cells with 10μM FT1050 for 2 hrs at 37°C resulted in greater proliferation with a statistically significant increase in colony formation, 11.5±1.4, compared to 4±0.8 colonies with DMSO control ($p < 0.001$). This short-term ex vivo incubation protocol, 10μM FT1050 for 2 hrs at 37°C, has been introduced into an ongoing Phase Ib clinical trial in adults with hematologic malignancies receiving a nonmyeloablative conditioning (melphalan, fludarabine and ATG) followed by double hCB transplantation, in which one of the two hCBs is incubated with FT1050 prior to infusion. The primary objective of the study is to determine the safety of FT1050 treatment of hCB. Preliminary data demonstrate that this ex vivo incubation can be reliably performed at the clinical site on the day of infusion with good cell recovery and viability. 11 subjects with a median age of 44 years have been accrued to date, of which two have been treated using the optimized ex vivo incubation protocol. 10 of 11 patients have achieved an ANC > 500 before Day 42. Transplant related mortality has been low with one death at Day 53 from respiratory failure. 9 patients are alive, of which 7 are disease-free. Accrual is ongoing.

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ALLOGENEIC TRANSPLANTATION USING HAPLOIDENTICAL DONOR VERSUS UNRELATED CORD BLOOD DONOR: A SINGLE CENTER RETROSPECTIVE STUDY

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We have performed a retrospective comparison of pediatric patients with leukemia receiving a haplo transplant (n = 29) or UCBT (n = 38) in Niño Jesus Children's Hospital since 1996 to 2010. There were not significant differences in immunophenotype, disease status and antecedent of prior autograft. However, haplo recipients tended to be older and of male gender.

Engraftment failure was significantly higher following UCBT 9±5% compared to 7±5% in haplo transplants (p = 0.001). Median neutrophil engraftment were at 13 days for haplo and 20 days for UCBT (p = 0.01) and platelet engraftment at 11 days for haplo and 56 days for UCBT (p = 0.0001). Supportive care (transfusions, antibiotics, parenteral nutrition and hospitalization days) were significantly higher for cord blood transplants.

TRM and acute GVHD (more than grade II) incidence was higher in UCBT compared to haplo transplants. There were not significant differences in chronic GVHD and relapse probability between the two groups. Results are summarized in table 1.

Disease-free survival (DFS) with a median follow-up of 16 months (range: 1-42) and 57 months (range: 1-150) were of 44±10% and 32±7% (p = 0.03) for haplo transplants and UCBT respectively. When we analyzed AML, there were not differences in DFS with both type of donor (p = 0.6). However, DFS for ALL was better with haplo (41±13%) against cord blood (26± 9%) (p = 0.03). According to phase of disease, DFS was similar in early phase (p = 0.7), but in advanced phase outcome was better with haplo (37±14%) versus cord blood (21±8%) (p = 0.05).

Multivariate analysis of DFS showed that the main prognostic factors were disease status at transplant (HR 2.49, p = 0.02), chronic GVHD (HR 0.21, p = 0.0001) and source of stem cells (HR 5.75, p = 0.001).

In conclusion, our data suggest that haploidentical donor is a good alternative for patients lacking an HLA identical donor.

Table 1. Results.

	aGVHD >II	TRM	Relapse	DFS
Haplo (n=29)	19±7%	25±9%	48±12%	44±10%
UCB (n=38)	44±10%	57±9%	25±9%	32±7%
P	0.03	0.05	0.7	0.03

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CD34+ STEM CELL SELECTION AND CD3+ ADDBACK FOR PEDIATRIC RECIPIENTS OF MATCHED UNRELATED ADULT DONOR (MUD) PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (PBSCT) PRELIMINARY RESULTS OF DAY 100 TRM, IMMUNE RECONSTITUTION (IR), PTLD, SYSTEMIC VIRAL INFECTIONS (SVI), AND INVASIVE FUNGAL INFECTIONS (IFI)

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Background: CD34+ stem cell selection depletes T cells responsible for severe aGVHD (Lang et al., Blood, 2003). CD34+ selected grafts have been associated with delayed IR (Ball et al, BMT, 2005, Eyrich et al, BJH, 2001). Delayed IR is a significant risk factor for